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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 10/540,503 | 07/25/2005 | Yasuhiro Kajihara | TAM-053 | 2741 |
| 20374 7590 03/01/2007 KUBOVCIK & KUBOVCIK SUITE 710 900 17TH STREET NW WASHINGTON, DC 20006 | | | EXAMINER | |
| | | | BLAND, LAYLA D | |
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| SHORTENED STATUTORY PERIOD OF RESPONSE | | MAIL DATE | DELIVERY MODE | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|------------------------------|------------------------|---------------------|--|
| | 10/540,503 | KAJIHARA ET AL. | |
| Examiner | Art Unit | | |
| Layla Bland | 1609 | | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 23 June 2005.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-22 and 24-28 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) 21 and 22 is/are allowed.

6) Claim(s) 1-20 and 24-28 is/are rejected.

7) Claim(s) 1,2 and 17-20 is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 6/23/05; 1/3/06.
4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ .
5) Notice of Informal Patent Application
6) Other: ____ .

DETAILED ACTION

The preliminary amendment of June 23, 2005 is acknowledged. Claim 23 is cancelled. Claims 1-22 and 24-8 are pending and examined on the merits herein.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The IDS of January 3, 2006 included non-English documents. Only the English abstract of document "DA" was considered and document "DB" was not considered.

Specification

The use of the trademarks Iatron, Sephadex and Cosmosil has been noted in this application. Trademarks should be in all capital letters or denoted with ™ or ®.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claims 17 and 18 are objected to because "asparagine" is incorrectly spelled as "aspareagine." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 19, 20 are rejected under 35 U.S.C. 112, second paragraph for lack of antecedent basis. As written, claim 2 is dependent on claim 1; however claim 2 is drawn to the α 2,6-oligosaccharaide derivative, which is a different compound from the α 2,3-oligosaccharide of claim 1. As written, claim 19 is dependent on claim 1; however the compounds involved in the process of claim 19 are not found in claim 1. As written, claim 20 is dependent on claim 2; however the compounds involved in the process of claim 20 are not found in claim 2.

Claims 1 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites that the compound of formula (1) must contain fluorine, but if R, R', and R" are all OH as described in (d), the resulting compound does not contain fluorine.

Claims 9-12 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the claims is drawn to a process wherein the structure of the starting material and the product appears to be identical. For example, in claim 9, which is drawn to a process of preparing a compound represented by the formula (14) by hydrolyzing a compound represented by formula

(13), the compounds of formulae (13) and (14) as given in the claim have the same structure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-8 and 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin, et al (Bioorganic & Medicinal Chemistry 1995, Vol. 3, No. 12, pp. 1625-1630) in view of Inazu, et al (Peptide Science 1999, vol. 1998, pp. 153-156) and further in view of Iida, et al (US 5,627,290, 1997).

Claims 1-6 are drawn to fluorine-containing asparagine-linked α 2,3- and α 2,6-oligosaccharide derivatives wherein the fluorine is on the sialic acid moiety. Claims 7 and 8 are drawn to a process for preparing asparagine-linked α (2,3)-disialooligosaccharide or monooligosaccharide derivatives. Claims 24-28 are drawn to an asparagine-linked α 2,6-oligosaccharide derivative containing fucose and process of preparing same.

Lin, et al. teach the preparation of asparagine-linked sugar chains similar to those in claims 1-8 via the transfer of sialic acid to an asparagine-linked oligosaccharide using α 2,3-sialyltransferase to afford the disialooligosaccharide [Figure 4, entries 1 and 3]. The disialooligosaccharide was obtained in 74% yield, and the formation of

monosialooligosaccharide in addition to the disialooligosaccharide is very likely. Lin, et al. teach the use a1,3-fucosyltransferase to prepare an α 2,3-oligosaccharide derivative containing fucose [Figure 4, entry 4]. Lin, et al also teach an α 2,6-oligosaccharide which does not contain fucose.

The sugar chains of Lin, et al. do not contain fluorine and are not protected with Fmoc.

Inazu, et al teach the introduction of an Fmoc group onto glycosylasparagine in order to facilitate purification [page 154, lines 1-5]. Inazu, et al do not teach the derivatives of claims 1-8 and 24-28.

Iida, et al teach fluorine-containing derivatives of sialic acid and their various physiological activities, including sialidase inhibition and carcinostatic action [columns 1 and 2, Related Art]. Iida, et al do not teach the derivatives of claims 1-8 and 24-28.

One of ordinary skill in the art would be motivated to combine the teachings in order to obtain derivatives of the glycosylasparagine of Lin, et al. with easier purification (as taught by Inazu, et al [page 154, lines 1-5]) and further physiological activities (as taught by Iida, et al [columns 1 and 2, Related Art]). Furthermore, application of the α 1,3-fucosyltransferase to the α 2,6-oligosaccharide as well as the α 2,3-oligosaccharide to obtain an α 2,6-oligosaccharide containing fucose would be well within the ordinary skill in the art.

Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unverzagt, et al (Tetrahedron Letters 1997 vol. 38, no. 32, pp. 5627-5630) in view

of Inazu, et al (Peptide Science 1999, vol. 1998, pp. 153-156) and further in view of Iida, et al (US 5,627,290, 1997).

Claims 12 and 13 are drawn to a process for preparing asparagine-linked α (2,6)-disialooligosaccharide or monosialooligosaccharide derivatives.

Unverzagt, et al. teach the preparation of asparagine-linked α 2,6 disialooligosaccharide derivatives via α 2,6-sialyltransferase followed by chromatography [Figure 3 and page 5629, lines 4-6]. Unverzagt, et al. also teach 3% of the monosialylated compound was obtained [page 5629, lines 4-6].

Unverzagt, et al does not teach a fluorinated derivative or a lipophilic protecting group.

Inazu, et al teach the introduction of an Fmoc group onto glycosylasparagine in order to facilitate purification [page 154, lines 1-5]. Inazu, et al. do not teach the derivatives of claims 12 and 13.

Iida, et al teach fluorine-containing derivatives of sialic acid and their various physiological activities, including sialidase inhibition and carcinostatic action [columns 1 and 2, Related Art]. Iida, et al do not teach the derivatives of claims 12 and 13.

One of ordinary skill in the art would be motivated to modify the compounds of Unverzagt, et al. in order to take advantage of easier purification as taught by Inazu, et al [page 154, lines 1-5] and to obtain compounds with further physiological activities, as taught by Iida, et al [columns 1 and 2, Related Art].

Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unverzagt, et al (Tetrahedron Letters 1997 vol. 38, no. 32, pp. 5627-5630).

Claims 17 and 18 are drawn to the preparation of asparagine-linked α 2,3- and α 2,6 oligosaccharides of formulae (9) and (10) via removal of the protecting group of compounds (6) and (8).

Unverzagt, et al. teach the removal of Fmoc from the asparagine residue of an asparagine-linked oligosaccharide derivative using piperidine.

Unverzagt, et al. do not teach the fluorinated derivatives of claims 17 and 18.

One of ordinary skill in the art would be motivated to remove the Fmoc protecting group from an asparagine-linked oligosaccharide in order to change the functionality of the molecule. For example, Unverzagt, et al. removed Fmoc in order to elongate the chain [figure 2 and page 5628, first paragraph].

Claims 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meinjohanns, et al. (J. Chem. Soc. Perkin Trans. I, 1998, pages 549-560).

Claims 19 and 20 are drawn to a process for preparing oligosaccharides of formulae (10) and (11) via the removal of the asparagine residue of compounds of formulae (8) and (9).

Meinjohanns, et al. teach hydrazinolysis for the release of N-linked oligosaccharides [page 551, scheme 2 and page 552, scheme 3].

Meinjohanns, et al. do not teach hydrazinolysis of the specific compounds of claims 19 and 20.

One of ordinary skill in the art would be motivated to carry out the hydrazinolysis of Meinjohanns, et al. in order to obtain the N-linked oligosaccharide in its intact unreduced form from the natural glycoproteins as taught by Mainjohanns, et al [abstract].

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4 and 6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18 and 19 of U.S. Patent No. 7,135,566 B2 in view of Iida, et al, US 5,627,290, 1997.

Claims 4 and 6 are drawn to a 2,6-oligosaccharides, containing fluorine, with and without asparagine.

Claims 18 and 19 of U.S. Patent No. 7,135,566 B2 are drawn to a 2,6-oligosaccharides with and without asparagine, and without fluorine.

Iida, et al teach fluorine-containing derivatives of sialic acid and their various physiological activities, including sialidase inhibition and carcinostatic action [columns 1 and 2, Related Art].

Although the conflicting claims are not identical, they are not patentably distinct from each other because it would be obvious to one of ordinary skill in the art to apply the teachings of Iida, et al. to Claims 18 and 19 of U.S. Patent No. 7,135,566 B2 in order to obtain compounds with further physiological activities.

Claims 21 and 22 are found to be allowable as they are drawn to novel compounds.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Bland whose telephone number is (703) 272-9572. The examiner can normally be reached on M-F 7:30AM-5:00PM UST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ldb

Cecilia Tsang
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SUPERVISORY PATENT EXAMINER